Application No.: 09/676,053 17044CPADIV (BOT)

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## **AMENDMENTS**

## Amendments to the Claims

1-30. (Canceled)

31. (Currently amended) A composition comprising an active Clostridial neurotoxin joined to a drug or other bioactive molecule:

wherein the active neurotoxin has binding specificity for a target nerve cell, is internalizable by the target nerve cell and has enzymatic activity for a target substrate selected from the group consisting of SNAP-25. VAMP and Cellubrevin.

- (Currently amended) The composition of claim 31 wherein said the active Clostridial neurotoxin is an active Clostridial botulinum neurotoxin
- 33. (Cancelled)
- 34. (Previously presented) The composition of claim 31 wherein said drug is an intracellular acting drug.
- 35. (Currently amended) The composition of <u>claim 31 claim 32</u> wherein said Clostridial neurotoxin is selected from the group consisting of <u>tetanus toxin</u>, <u>a</u> botulinum toxin A, <u>a</u> botulinum toxin B, <u>a</u> botulinum toxin C1.[[;]] <u>a</u> botulinum toxin D, <u>a</u> botulinum toxin E, <u>a</u> botulinum toxin F, and <u>a</u> botulinum toxin G.
- 36. (Previously presented) The composition of claim 31 wherein said drug is selected from the group consisting of: a protein synthesis toxin, an inhibitor of neurotransmitter release, a neuronal calcium channel blocker, a ribozyme and an oligonucleotide.
- (New) The composition of claim 31 wherein the active Clostridial neurotoxin is an active tetanus neurotoxin.

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38. (New) A pharmaceutical composition for treatment of a neuromuscular dysfunction in a mammal, comprising an active Clostridial neurotoxin joined to a drug or other bioactive molecule; and a pharmaceutically acceptable excipient;

wherein the active neurotoxin has binding specificity for a target nerve cell, is internalizable by the target nerve cell and has enzymatic activity for a target substrate selected from the group consisting of SNAP-25, VAMP and Cellubrevin.

- (New) The pharmaceutical composition of claim 38 wherein the active Clostridial neurotoxin is an active botulinum neurotoxin.
- 40. (New) The pharmaceutical composition of claim 39 wherein the active botulinum neurotoxin is selected from the group consisting of a botulinum toxin A, a botulinum toxin B, a botulinum toxin C1, a botulinum toxin D, a botulinum toxin E, a botulinum toxin F, and a botulinum toxin G.
- 41. (New) The composition of claim 38 wherein the active Clostridial neurotoxin is an active tetanus neurotoxin
- 42. (New) The pharmaceutical composition of claim 38 wherein the neuromuscular dysfunction is characterized by uncontrollable muscle spasms.
- 43. (New) The composition of either of claims 31 or 38 wherein the drug or other bioactive molecule is an inhibitor of neurotransmitter release.
- 44. (New) The composition of either of claims 31 or 38 wherein the drug or other bioactive molecule is an active ingredient for treatment of botulism or tetanus.
- 45. (New) The composition of either of claims 31 or 38 wherein the drug or other bioactive molecule is selected from the group consisting of a GABA agonist, a neuronal calcium channel agonist, an adenosine agonist, a glutamate antagonist, a protein synthesis toxin, a zinc-dependent protease inhibitor, a neuronal growth factor, an antiviral agent, a

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nicotinic antagonist, a neuronal calcium channel blocker, an acetylcholine esterase inhibitor, a potassium channel activator, a vasamicol or a vasamicol inhibitor, a ribozyme, and a transcribable gene.